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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/610,891	07/06/2000	James McArthur	40567	6712

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EXAMINER	
YU, MISOOK	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 02/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/610,891	MCARTHUR ET AL.	
	Examiner	Art Unit	
	MISOOK YU, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/20/2003 has been entered.

Claims 35, 38, 39, 41, and 42 are amended, and claim 43 is new. Claims 35-43 are pending and examined on merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

This Office action contains new grounds of rejections.

Response to Argument

Claim Rejections - 35 USC § 112

Claims 35-42 **remain rejected** and the new claim 43 is also rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the **written description** requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification at page 16 lines 14-19 says instant invention to be a composition comprising "cells transduced with DNA ... expressing **at least an immunogenic portion of a novel tumor-associated antigen**." Therefore, the Office

interprets the claims as drawn to composition comprising a proliferation-incompetent cell comprising transduced DNA encoding a prostate tumor-associated antigen identified as only western-blot-determined molecular weight of 250 kD (Figs. 5 to 7), 160 kD (Figs. 5 to 7), 150 kD (Figs. 2 to 4), 31 kD (Fig. 2), 26 kD (Fig. 2) or 14 kD (Figs. 5 to 7).

Applicant argues the claims recite particular prostate tumor antigens, with a molecular weight of 250 kD (Figs. 5 to 7), 160 kD (Figs. 5 to 7), 150 kD (Figs. 2 to 4), 31 kD (Fig. 2), 26 kD (Fig. 2) or 14 kD (Figs. 5 to 7) shown in Western blots wherein specific antisera bind to prostate tumor antigens that were not detectable prior to exposure to proliferation-incompetent prostate tumor cells and GM-CSF; the current claims are supported by the description at least on page 7, lines 19-27, page 9, lines 12-19 for proliferation-incompetent, page 9, lines 26-27 (GM-CSF), page 10, lines14-15 (autologous), page 10, lines 18-19 (allogeneic), and page 10, lines 32-34 (prostate cancer); an artisan would well recognize that the inventors were in possession of the claimed invention on reading the instant specification. These arguments have been fully considered but found not persuasive because one has to know the chemical structure of the DNA molecule encoding that the novel tumor-associated antigens in order to make a proliferation-incompetent cells transduced with DNA encoding an immunogenic portion of said novel tumor-associated antigens. However, the specification does not teach identity of any nucleic structure encoding 250, 160, 150, 31, 26, or 14 kDa antigens. Note page 24 line 30 of the specification that discloses the

epitopes to the anti-sera are unknown. Thus, applicant does not have possession of the nucleic acid encoding structure encoding 250, 160, 150, 31, 26, or 14 kDa antigens.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is molecular weights of different antigens of cancer cell lines detected with anti-sera generated in cancer patients who received GVAX. Accordingly, in the absence of the DNA structure necessary in order to transduce proliferation-competent cells, the specification does not provide adequate written description.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed the nucleic acid molecule structures encoding the 6 novel-tumor associated antigens, given that the specification has only described molecular weight based on Western blot. The nucleic acid molecules encoding the 6 novel antigens has

yet to be determined. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is separable from its enablement provision (see page 1115). As for applicant argument that the antigens appear only in presence of GM-CSF, A definition by function alone "does not suffice, to sufficiently describe a coding sequence "because it is only an indication of what the gene does, rather than what it is." *Eli Lily*, 119 F.3 at 1568, 43 USPQ2d at 1406.

Claim Rejections - 35 USC § 102

Claims 35-42 **remain rejected** for reason of record and new claim 43 is also under 35 U.S.C. 102(b) as being anticipated by Dranoff, et al. (US Pat. 5,637,483, June. 10 1997).

The claims are interpreted as drawn to **composition per se** comprising a proliferation-incompetent cell (the base claim 35, claim 39), a proliferation-incompetent autologous cell (claim 36), a proliferation-incompetent allogeneic cell (claim 37), a proliferation-incompetent cell expressing with GM-CSF expression vector (claim 38), a proliferation-incompetent prostate cell (claim 40), proliferation-incompetent cell plus a host cell (claim 41), proliferation-incompetent cell plus non-cancerous cell expressing GM-CSF (claim 42), and proliferation-incompetent cell plus other cells expressing GM-CSF (claim 43).

Applicant argues that the instant invention as recited in the base claim relates to prostate tumor antigens which alone do not stimulate a humoral response, but when administered with a proliferation-incompetent cell in the presence of GM-CSF provided by GVAX vaccine, are effectively immunogenic and responds to that prostate tumor

antigen, in part, by generating antibody and Dranoff et al does not teach the particular prostate tumor antigens having the claimed molecular weight and immunological characteristics. These arguments have been fully considered but found unpersuasive for following: First, applicant's attention is directed at the limitation of instant claims, the claims do not say anything about GVAX vaccine. Therefore the argument with GVAX vaccine is considered as arguing a limitation not present in the claim. As for the argument that Dranoff et al does not teach the particular prostate tumor antigens having the claimed molecular weight and immunological characteristics, it appears that any cancer cells (see the instant Figs. 2-7) have such antigens when GVAX vaccine is administered to patients.

The specification discloses that applicant's discovery is the several bands (250, 160, 150, 31, 26, 14 kDa) seen on Western blot prepared by lysates of cancer cells lines (see Figs. 2-7) reacted with sera of patient who have received GVAX vaccine. It appears any cancer cells have such characteristics inherently when they are stimulated with GVAX vaccine. It appears that any cancer cells have such potential once stimulated by GM-CSF, according to the second paragraph of page 24 of the instant specification.

Applicant is invited to present scientific evidence to the Office that the composition comprising **proliferation-incompetent cell** transduced with GM-CSF disclosed in claims 1-17 of Dranoff et al do not possess such characteristic when administered to patients in order to obviate this rejection.

Claims 35-42 remain rejected for reason of record and claims 43 is also rejected under 35 U.S.C. 102(a) as being anticipated by Hiserdodt, et al., (WO 98/04282, 1998).

Applicant argument that Hiserdodt et al do not teach the particular prostate tumor antigens but this argument is not persuasive for reasons given above (see 102 rejection) in rejection of instant claims by Dranoff et al.

The Following are New Grounds of Objections and Rejections

Specification

The use of the trademark GVAX, for example at page 21 line 6, has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Response to Amendment

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 42 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 42 recites the limitation "said GM-CSF-expressing cell" in 2. There is insufficient antecedent basis for this limitation in the claim.

Claims 35-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the **enablement** requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are interpreted as drawn to a composition comprising a proliferation-incompetent cell comprising DNA encoding a prostate tumor-associated antigen identified as only western-blot-determined molecular weight of 250, 160, 150, 31 kD, 26 kD, or 14 kD. The entire specification is about applicant's discovery of 6 new bands (namely 250, 160, 150, 31, 26, 14 kDa) seen on Western blot prepared by lysates of cancer cells (see Figs. 2-7) reacted with sera of patient who have received GVAX vaccine i.e., melanoma cells incorporating the granulocyte macrophage colony stimulating factor (GM-CSF) gene according to O'Rourke et al., Aust N Z J Surg. 1997 Dec;67(12):834-41. However, the specification does not teach any proliferation-incompetent cell comprising a nucleic acid encoding prostate tumor-associated antigen with the characteristics of base claim 35. The cells inside the patients who had received GVAX vaccine as disclosed in instant Fig. 2-7 must have expressed immunogenic antigens of 250, 160, 150, 31, 26, 14 kDa in order to generate the antibodies. The cells inside human body does not appear to be proliferation incompetent. In order to make proliferation-incompetent the cells, one has be to irradiated cells (see claim 1 of the

Dranoff et al, art of record, see also 102 rejection above). It is not clear whether irradiated cancer cells would have such characteristics or only cancer cells in live human without irradiation have such characteristics. The specification does not describe any cells taken out of human body and then irradiated would have such characteristics i.e., the 6 antigens are immunogenic in presence or absence of GM-CSF.

Walczak et al (Expert Opin Investig Drugs. 2002 Dec; 11(12): 1737-48, abstract only) and Dummer (Curr Opin Investig Drugs. 2001 Jun; 2(6):844-8, abstract only) are cited to show the current state of art regarding the nature of immune response to GVAX. Dummer teaches that clinical trial using GVAX vaccine for prostate cancer results in an increased quantity of immune system stimulant. Walczak et al also teach GVAX vaccine is used for prostate cancer. Neither the specification nor the art teach the identity of the immunogenic antigens when patient's immune system is stimulated with GVAX vaccine. Therefore such antigens have yet to be identified, which requires a large quantity of experimentation. In order to make the instantly claimed composition, one first has to know the nucleic acid sequences of the antigens represented by 250, 160, 150, 31, 26, 14 kDa. The claims do not say anything about whether the identical antigens are expressed in all hosts of entire animal kingdom or just phenomena in human only. If the antigens are expressed in other animals than humans, it is not clear whether the same antigens with same sizes would be expressed. Based on the teachings of the specification, it is not clear whether the 6 different bands come from single protein or multiple proteins. The specification does not teach whether the immune response in

patients who received GVAX vaccine came from overexpression of the 6 antigens or other immunogenic events such as shedding of certain parts of the antigens.

O'Keefe et al (Prostate. 2004 Feb 1; 58(2): 200-10) is cited to show that determining nucleic acid sequence of interest (cloning cDNA of interest) even with information regarding which primers (see page 201) to use requires a large quantity of experiments (see Table I, II and Figs 1-7). Instant case, one has to figure out the identity of the antigens of 250, 160, 150, 31, 26, 14, then figure out what kind of primers to use the clone the nucleic acids of instantly claimed cell comprises of. Considering the limited guidance in the specification how to make cell comprising unknown nucleic acid molecule encoding 250, 160, 150, 31, 26, 14 kDa and unpredictability in the cDNA cloning art, it is determined that undue experimentation is required in order to practice the instantly claimed invention.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 571-272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eyler C Yvonne can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Misook Yu
January 22, 2004

LARRY R. HELMS, PH.D
PRIMARY EXAMINER